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EXAMINER	
BAUM, STUART F	

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1638	12

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/890,220	Applicant(s) DEAN ET AL.	
	Examiner Stuart F. Baum	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 60-106* is/are pending in the application.

4a) Of the above claim(s) *5-10,66-71,76,77 and 79-106* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,60-65,72-75 and 78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *with the application* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Claims 1-10, and 60-106 are pending.

2. Applicant's election with traverse of Group I, claims 1-4, 60-65, 72-75 and 78, including SEQ ID NO:1 and 2, in Paper No. 11 is acknowledged. The traversal is on the ground(s) that it is improper to make a lack of unity holding in a §371 application, when the international application was found to have unity. Applicant cites Example 17 of the Annex which states that there exists a special technical feature for one DNA sequence encoding one protein (page 8, middle paragraph). Applicant continues by contending that the US Examiner has improperly applied the rules for unity of invention. In particular, Applicants contend that the Chandler (1996) reference does not pertain to cloning or transcription of VRN2 or even a fragment thereof and even if Chandler did affect claim 105, Applicants contend that this is irrelevant to claims 1 and 2 and the inventive concept which unifies the various groups defined by the Examiner. Applicants also contend that the submitted sequences are not unrelated to each other and in fact SEQ ID NO:1 and 4, which are the VRN2 cDNA sequences from *Arabidopsis thaliana* Landsberg erecta and Columbia, respectively, exhibit 96% sequence identity as determined by BLASTN. Applicants also state that SEQ ID NO:3 and 6 are the corresponding genomic sequences of the cDNA's of SEQ ID NO:1 and 4, and also exhibit large regions of homology. Lastly, Applicant contends that according to the MPEP, Applicant is entitled to up to four sequences be examined together.

3. This is not found persuasive because the Examiner did follow the rules for lack of unity of invention because Applicants' claims are drawn to many sequences, including variants and the

Example 17 as cited by Applicants refers to one DNA sequence encoding one amino acid sequence. Applicant has only provided an alignment for the DNA sequence but Applicant has not disclosed the sequence alignment for the corresponding amino acid sequences nor has Applicant addressed if the two corresponding pair of sequences have the same function. Given the lack of functional and complementation data, it is presumed that the corresponding amino acid sequences i.e., SEQ ID NO:2 and 5, are unrelated to each other. It is acknowledged that the genomic sequences exhibit some degree of sequence identity to the corresponding cDNA sequence, but genomic sequences also contain sequence information, i.e., introns, which renders the associated sequence a structurally and patentably distinct structure. Lastly, in regards to the permissible number of sequences as specified in the MPEP, those guidelines were for EST sequences which are much shorter than the nucleic acid sequences presented in the present application, and because of the vast number of sequences now present in the current databases that must be searched, the Office does not have the resources to search more than one corresponding pair of nucleic acid and amino acid sequences per application. And lastly, according to the MPEP, up to four sequences will be examined, and one sequence is considered up to four, for the reasons stated above.

4. Applicant is invited to petition the Commissioner to review the restriction requirement under 37 CFR 1.144. This petition must not be filed later than the filing of a Notice of Appeal.

5. The requirement is still deemed proper and is therefore made FINAL.

Claims 5-10, 66-71, 76-77, and 79-106 have been withdrawn from consideration because the claims are drawn to non-elected inventions.

6. Claims 1-4, 60-65, 72-75 and 78 are examined in the present office action.

Specification

7. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See for example page 11, line 12. See MPEP § 608.01.

Claim Objections

8. In claims 3 and 4 the abbreviation "NO." needs to have all letters capitalized.

Claims 60-61, 63-64, 72-75 and 78 are objected to for reading on non-elected inventions. Correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-4, 60-65, 72-75 and 78 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection includes dependent claims.

In claim 1, the metes and bounds of "obtainable" have not been defined. It is unclear what DNA is not encompassed in the recitation "obtainable". All subsequent recitations of "obtainable" are also rejected.

In claim 1, the recitation "VRN2 locus" has not been defined. Applicants have not specifically stated what nucleic acids are encompassed in the recitation "VRN2 locus".

In claim 1, the metes and bounds of "capable" have not been defined. What are the limits to which something is "capable". All subsequent recitations of "capable" are also rejected.

In claim 1, the metes and bounds of "affecting" have not been defined. Applicants have not specifically stated what are the upper and lower limits that are encompassed in the recitation "affecting". All subsequent recitations of "affecting" are also rejected.

In claim 1, the metes and bounds of "vernalization response" have not been defined. It is unclear what "responses" are included in the "vernalization" process. All subsequent recitations of "vernalization response" are also rejected.

In claim 60, the recitation "variant" has not been defined. Applicant needs to explicitly state what is encompassed by the recitation "variant". All subsequent recitations of "variant" are also rejected.

In claim 60, the recitation "homologous" has not been defined. The meaning of the word "homologous" includes an evolutionary component, that is not defined.

In claim 60, 5th line, the word "sequence" needs to be inserted before the word "identity".

In claim 63, replace the word "homology" with --sequence identity--. The meaning of the word "homology" includes an evolutionary component, that is not defined.

In claim 64, it is not clear if the phrase "which is a fragment of a sequence..." is only modifying SEQ ID NO:7 or is intended to modify all of the preceding SEQ ID NO's which would include SEQ ID NO:1.

In claim 72, the metes and bounds of "partly" or "substantially" have not been defined. The Office interprets these terms to mean one base pair. All subsequent recitations of "partly" or "substantially" are also rejected.

In claim 74, 2nd line, insert the word "to" before the word "claim".

In claim 75, the recitation of "conditions for hybridisation" has not been defined. Applicants have not taught the specific conditions that must be used to facilitate hybridization of the probe with the desired nucleic acid sequence.

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-2, 60-63, 65, 72-75, and 78 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants claim an isolated nucleic acid obtainable from the VRN2 locus of any plant, a variant sequence of SEQ ID NO:1 and which shares at least 50% sequence identity therewith, an allelic variant of SEQ ID NO:1, a variant VRN2 sequence from any plant other than *Arabidopsis*, or a derivative sequence of SEQ ID NO:1 wherein said sequence has additions, insertions, deletions or substitutions of any nucleotide(s) and wherein said derivative sequence shares at least 50% sequence identity with SEQ ID NO:1. The Applicants also claim a method for

identifying or cloning a nucleic acid, or a method for determining the presence of a nucleic acid, both methods comprising a variant sequence of SEQ ID NO:1 which shares at least 50% sequence identity therewith, or a sequence consisting of SEQ ID NO:1, comprising using a probe or primer that is partly, substantially or completely conserved between two or more VRN2 sequences specified in claim 72. Lastly, Applicants claim a method of selecting a plant having a desired allele of the VRN2 gene comprising a probe or primer encoding an amino acid sequence that is partly, substantially or completely conserved between a VRN2 sequence of SEQ ID NO:2 and another non-elected sequence, wherein said nucleic acid is 15 to 40 nucleotides in length.

The specification only discloses the nucleic acid sequence of SEQ ID NO:1 purportedly encoding SEQ ID NO:2, but Applicants do not specify the start or stop codons of SEQ ID NO:1 so it is unclear from the specification if in fact Applicants have provided the full length nucleic acid sequence that encodes SEQ ID NO:2. In addition, Applicants do not disclose any specific structural, physical and/or chemical properties for the claimed sequence. Applicants do not present a description of domains that are specific to this particular protein nor domains that are important for its proper function. Applicants also do not define the nucleic acid sequence explicitly associated with the VRN2 locus of any plant. Given the lack of description of the before mentioned sequences, one skilled in the art would not be able to identify sequences with less than 100% sequence identity that still maintained the proper activity. The claims recite variant sequences and sequences which share at least 50% sequence identity with SEQ ID NO:1 or sequences that are partly, or substantially conserved between any two sequences mentioned in, for example, claim 72, but Applicant has not disclosed a representative number of species as encompassed by the claims. The claims encompass mutants and allelic variants and thus imply

that structural variants exist in nature, yet no structural variant has been disclosed. The implication is that there is a gene and a protein other than that disclosed which exists in nature, but the structure thereof is not known. Thus, there are insufficient relevant identifying characteristics to allow one skilled in the art to predictably determine such mutants and allelic variants from other plants and organisms, absent further guidance. Therefore, the written description requirement is not satisfied. Therefore, one skilled in the art would not recognize from the disclosure that Applicant was in possession of the claimed invention. (See Written Description Requirement published in Federal Register/Vol.66, No. 4/ Friday, January 5, 2001/Notices; p. 1099-1111).

Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1-4, 60-65, 72-75 and 78 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants claim an isolated nucleic acid obtainable from the VRN2 locus of any plant, a variant sequence of SEQ ID NO:1 and which shares at least 50% sequence identity therewith, an allelic variant of SEQ ID NO:1, a variant VRN2 sequence from any plant other than *Arabidopsis*, or a derivative sequence of SEQ ID NO:1 wherein said sequence has additions, insertions,

deletions or substitutions of any nucleotide(s) and wherein said derivative sequence shares at least 50% sequence identity with SEQ ID NO:1. The Applicants also claim a method for identifying or cloning a nucleic acid, or a method for determining the presence of a nucleic acid, both methods comprising a variant sequence of SEQ ID NO:1 which shares at least 50% sequence identity therewith, or a sequence consisting of SEQ ID NO:1, comprising using a probe or primer that is partly, substantially or completely conserved between two or more VRN2 sequences specified in claim 72. Lastly, Applicants claim a method of selecting a plant having a desired allele of the VRN2 gene comprising a probe or primer encoding an amino acid sequence that is partly, substantially or completely conserved between a VRN2 sequence of SEQ ID NO:2 and another non-elected sequence, wherein said nucleic acid is 15 to 40 nucleotides in length.

Applicants isolated two *Arabidopsis vrn2* mutant alleles by mutagenising *fca-1* seeds (page 46, lines 15-21) and mapped the *VRN2* gene to chromosome IV (page 48, line 20). Two cosmids, IB4A23 and IB6N1, were able to complement the mutation (page 50, line15). Applicants used RT-PCR using total RNA prepared from *fca-1, vrn2-1 fca-1* and *vrn2-2 fca-1* 14 day old seedlings and also using primers designed to amplify products encompassing the entire predicted open reading frame of putative genes, 5K and 4450 (page 51, lines 22-37) to eventually clone the *VRN2* gene.

Applicants have not reduced to practice their invention. Applicants have not taught how one skilled in the art can make and/or use the broadly claimed sequences to affect one or more physical characteristics of a plant into which the nucleic acid is introduced, the physical characteristics being selected from vernalization response, flowering time, leaf size and/or shape or shade avoidance response. In addition, Applicants have not taught a method for identifying or

cloning any of the nucleic acid sequences mentioned above using a probe or primer as claimed above. Applicants have also not taught a method for determining the presence of a nucleic acid as specified in claim 60 using a probe or primer as claimed above using the unspecified conditions for hybridization as claimed in claim 75. And lastly, Applicants have not taught a method of selecting a plant having a desired allele of the VRN2 gene using a probe or primer as specified above.

Applicants are claiming a nucleic acid from the VRN2 locus of any plant but Applicants have not specified a particular nucleic acid sequence associated with the VRN2 locus in the claim language. Applicants teach another nucleic acid sequence exhibiting "significant similarity to a predicted *Arabidopsis* protein which is quite close to VRN2 on chromosome 4, only 30 kb away..." (page 54, lines 20-23). Applicants contend that the predicted protein has can have a greater sequence identity to VRN2 if a different splice site is used. The main point of this discussion is that there are a number of nucleic acid sequences encoding proteins associated with the VRN2 locus, and Applicants have not specifically specified to which sequence they are referring when using the nomenclature "VRN2 locus".

It cannot be predicted by one of skill in the art that nucleic acids that are variant sequences, sequences exhibiting 50% sequence identity to SEQ ID NO:1, derivatives of variant sequences, or fragments of SEQ ID NO:1, will encode a protein with the same activity as SEQ ID NO:2. Bowie et al (1990, Science 247:1306-10) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of the protein to fold into unique three-dimensional structures that allows it to function and carry out the instructions of the genome. The cited reference also teaches that the prediction of protein

structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein, is extremely complex (pg 1306, left column). Bowie et al teach that while it is known that many amino acid substitutions are possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship, and these regions can tolerate only conservative substitutions or none at all (pg 1306, right column). The sensitivity of proteins to alterations in even a single amino acid in a sequence is exemplified by McConnell et al (2001, Nature 411 (6838):709-713), who teach that the replacement of a glycine residue located within the START domain of either the PHABULOSA or PHAVOLUTA protein receptor with either an alanine or aspartic acid residue, alters the sterol/lipid binding domain. This change renders the protein constitutively active and therefore creates a dominant mutation which has a drastic alteration in phenotype compared to wild-type *Arabidopsis* plants.

Applicant's claims are drawn to methods for identifying or cloning a nucleic acid sequence, methods for determining the presence of a nucleic acid, or a method of selecting a plant having a desired allele of the VRN2 gene, all of which comprise using a probe or primer that is partly, substantially, or completely conserved between a VRN2 of SEQ ID NO:2 and at least one other non-specified sequence. In claim 75, Applicants do not disclose the specific hybridization conditions required to for isolating the desired sequence. The state-of-the-art teaches isolating DNA fragments even using stringent hybridization conditions, does not always select for DNA fragments whose contiguous nucleotide sequence is the same or nearly the same as the probe. Fourgoux-Nicol et al (1999, Plant Molecular Biology 40 :857-872) teach the

isolation of a 674bp fragment using a 497bp probe incorporating stringent hybridization conditions comprising three consecutive 30 minute rinses in 2X, 1X and 0.1X SSC with 0.1% SDS at 65^0C (page 859, left column, 2^{nd} paragraph). Fourgoux-Nicol et al also teach that the probe and isolated DNA fragment exhibited a number of sequence differences comprising a 99bp insertion within the probe and a single nucleotide gap, while the DNA fragment contained 2 single nucleotide gaps and together the fragments contained 27 nucleotide mismatches. Taking into account the insertions, gaps and mismatches, the longest stretch of contiguous nucleotides to which the probe could hybridize consisted of 93bp of DNA (page 862, Figure 2). In the present example, the isolated fragment exhibits less than 50% sequence identity with the probe. One would expect that using probes or primers that are partly, or substantially conserved with respect to the gene of interest, will identify even a greater number of sequences that are outside the scope of the claims.

Claims 72-75 and 78 are drawn to methods for identifying or cloning a nucleic acid sequence, methods for determining the presence of a nucleic acid, or a method of selecting a plant having a desired allele of the VRN2 gene, all of which comprise using a probe or primer that is partly, substantially, or completely conserved between a VRN2 of SEQ ID NO:2 and at least one other non-specified sequence. The state-of-the-art teaches that isolating or identifying nucleic acid sequences that exhibit sequence identity with each, does not always identify sequences encoding proteins with the same activity. Bowman et al (1999, Development 126:2387-2396) teach the identification of four genes with sequence similarity to the *CRABS CLAW* (*CRC*) gene (page 2390, Figure 4) and are included in the same family as *CRC*. Siegfried et al (1999, Development 126:4117-4128) teach the function of the other family

members, whose function is different than *CRC* (page 4118, right column, last paragraph; page 4123, right column, first paragraph of DISCUSSION compared with Bowman et al., page 2394, DISCUSSION).

Applicant's claims are drawn to sequences that when transformed into a plant affect plant development. Transforming plants with heterologous genes that are involved in plant development produce unpredictable results. Kano-Murakami et al (1993, FEBS 334:365-368) teach introducing the *Oryza sativa* homeobox 1 (OSH1) gene into tobacco. OSH1 is a rice homologue of the *Knotted-1* homeobox gene from maize and would be encompassed by Applicant's broad claim language. Kano-Murakami et al teach transgenic tobacco plants comprising the OSH1 gene display a "range of phenotypes which include abnormalities in leaf and petal shape as well as stem height and number" (page 365, right column, 1st paragraph).

Given the claim breadth, unpredictability and lack of guidance as stated above; given the breadth of the claims which encompass a multitude of sequences that have not been exemplified; it would require undue experimentation by one skilled in the art to identify and isolate a multitude of non-exemplified nucleic acid sequences encoding polypeptides from a multitude of non-exemplified plants, and to evaluate the ability of these sequences, variants and derivative sequences thereof having the ability to cause the claimed effects in plants transformed therewith.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1-4, and 60-65, are rejected under 35 U.S.C. 102(b) as being anticipated by Schmidt et al (1995, Science 270:480-483).

Applicants claim an isolated nucleic acid obtainable from the VRN2 locus of any plant, a variant sequence of SEQ ID NO:1 and which shares at least 50% sequence identity therewith, an allelic variant of SEQ ID NO:1, a variant VRN2 sequence from any plant other than *Arabidopsis*, or a derivative sequence of SEQ ID NO:1 wherein said sequence has additions, insertions, deletions or substitutions of any nucleotide(s) and wherein said derivative sequence shares at least 50% sequence identity with SEQ ID NO:1.

Schmidt et al teach yeast artificial chromosome (YAC) clones comprising the DNA from chromosome 4, on which the VRN2 locus resides. Given that Schmidt et al had to isolate the DNA before constructing the YAC clones, and given that the VRN2 locus nucleic acid is obtainable from the YAC clones, Schimdt et al anticipate the claimed invention.

13. Claims 72-75 and 78 are deemed free of the prior art, given the failure of the prior art to teach or reasonably suggest a method for identifying or cloning a nucleic acid, a method for determining the presence of a nucleic acid and a method of selecting a plant having a desired allele of the VRN2 gene, all of which comprise a probe or primer comprising a nucleic acid sequence that is partly, substantially, or completely conserved with SEQ ID NO:1.

14. No claims are allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart Baum whose telephone number is (703) 305-6997. The examiner can normally be reached on Monday-Friday 8:30AM – 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 or (703) 305-3014 for regular communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist, who may be contacted at 308-0196.

Stuart F. Baum Ph.D.

August 8, 2003

DAVID T. FOX
PRIMARY EXAMINER
GROUP ~~180~~ 1638